

PATENT COOPERATION TREATY

PCT

NOTIFICATION OF ELECTION

(PCT Rule 61.2)

From the INTERNATIONAL BUREAU

To:

Commissioner
 US Department of Commerce
 United States Patent and Trademark
 Office, PCT
 2011 South Clark Place Room
 CP2/5C24
 Arlington, VA 22202
 ETATS-UNIS D'AMERIQUE
 in its capacity as elected Office

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| Date of mailing (day/month/year) 01 March 2001 (01.03.01) | Applicant's or agent's file reference EX99-004C-PCT |
| International application No. PCT/US00/15880 | Priority date (day/month/year) 14 June 1999 (14.06.99) |
| International filing date (day/month/year) 08 June 2000 (08.06.00) | |
| Applicant COSTA, Michael, A. et al | |

1. The designated Office is hereby notified of its election made:

☒ in the demand filed with the International Preliminary Examining Authority on:

05 January 2001 (05.01.01)

☐ in a notice effecting later election filed with the International Bureau on:
2. The election ☒ was
☐ was not

made before the expiration of 19 months from the priority date or, where Rule 32 applies, within the time limit under Rule 32.2(b).

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| The International Bureau of WIPO 34, chemin des Colombettes 1211 Geneva 20, Switzerland Facsimile No.: (41-22) 740.14.35 | Authorized officer Sean Taylor Telephone No.: (41-22) 338.83.38 |
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PATENT COOPERATION TREATY

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INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

REC'D 09 AUG 2001

WIPO

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| Applicant's or agent's file reference EX99-004C-PC | | FOR FURTHER ACTION See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416) | |
| International application No. PCT/US00/15880 | International filing date (day/month/year) 08 June 2000 (08.06.2000) | Priority date (day/month/year) 14 June 1999 (14.06.1999) | |
| International Patent Classification (IPC) or national classification and IPC IPC(7): A01K 67/00, 33/00; G01N 33/00 and US Cl.: 800/3, 8, 13 | | | |
| Applicant EXELIXIX, INC. | | | |
| <p>1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.</p> <p>2. This REPORT consists of a total of <u>5</u> sheets, including this cover sheet.</p> <p><input type="checkbox"/> This report is also accompanied by ANNEXES, i.e., sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).</p> <p>These annexes consist of a total of <u>0</u> sheets.</p> <p>3. This report contains indications relating to the following items:</p> <ul style="list-style-type: none"> I <input checked="" type="checkbox"/> Basis of the report II <input type="checkbox"/> Priority III <input checked="" type="checkbox"/> Non-establishment of report with regard to novelty, inventive step and industrial applicability IV <input type="checkbox"/> Lack of unity of invention V <input checked="" type="checkbox"/> Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement VI <input type="checkbox"/> Certain documents cited VII <input type="checkbox"/> Certain defects in the international application VIII <input checked="" type="checkbox"/> Certain observations on the international application | | | |
| Date of submission of the demand 05 January 2001 (05.01.2001) | | Date of completion of this report 15 July 2001 (15.07.2001) | |
| Name and mailing address of the IPEA/US Commissioner of Patents and Trademarks Box PCT Washington, D.C. 20231 Facsimile No. (703)305-3230 | | Authorized officer <i>Ram K. Shukla</i> Telephone No. (703) 308-0196 | |

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.

PCT/US00/15880

I. Basis of the report**1. With regard to the elements of the international application:***

- ☒ the international application as originally filed.
- ☒ the description:
pages 1-58 as originally filed
pages NONE, filed with the demand
pages NONE, filed with the letter of _____.
- ☒ the claims:
pages 59-62, as originally filed
pages NONE, as amended (together with any statement) under Article 19
pages NONE, filed with the demand
pages NONE, filed with the letter of _____.
- ☒ the drawings:
pages 1 and 2, as originally filed
pages NONE, filed with the demand
pages NONE, filed with the letter of _____.
- ☒ the sequence listing part of the description:
pages 1-22, as originally filed
pages NONE, filed with the demand
pages NONE, filed with the letter of _____.

2. With regard to the language, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

These elements were available or furnished to this Authority in the following language _____ which is:

- ☐ the language of a translation furnished for the purposes of international search (under Rule 23.1(b)).
- ☐ the language of publication of the international application (under Rule 48.3(b)).
- ☐ the language of the translation furnished for the purposes of international preliminary examination (under Rules 55.2 and/or 55.3).

3. With regard to any nucleotide and/or amino acid sequence disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

- ☒ contained in the international application in printed form.
- ☒ filed together with the international application in computer readable form.
- ☐ furnished subsequently to this Authority in written form.
- ☐ furnished subsequently to this Authority in computer readable form.
- ☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
- ☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. ☐ The amendments have resulted in the cancellation of:

- ☐ the description, pages NONE
- ☐ the claims, Nos. NONE
- ☐ the drawings, sheets/fig NONE

5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).**

* Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17).

** Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.

PCT/US00/15880

III. Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

1. The question whether the claimed invention appears to be novel, to involve an inventive step (to be non-obvious), or to be industrially applicable have not been and will not be examined in respect of:

- ☐ the entire international application,
☒ claims Nos. 8,9 and 22-31

because:

- ☐ the said international application, or the said claim Nos. _____ relate to the following subject matter which does not require international preliminary examination (*specify*):

- ☐ the description, claims or drawings (*indicate particular elements below*) or said claims Nos. _____ are so unclear that no meaningful opinion could be formed (*specify*):

- ☐ the claims, or said claims Nos. _____ are so inadequately supported by the description that no meaningful opinion could be formed.

- ☒ no international search report has been established for said claims Nos. 8, 9, and 22-31

2. A meaningful international preliminary examination cannot be carried out due to the failure of the nucleotide and/or amino acid sequence listing to comply with the standard provided for in Annex C of the Administrative Instructions:

- ☐ the written form has not been furnished or does not comply with the standard.
☒ the computer readable form has not been furnished or does not comply with the standard.

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.

PCT/US00/15880

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. STATEMENT

| | | |
|-------------------------------|-----------------------------|-----|
| Novelty (N) | Claims <u>1-7 and 10-21</u> | YES |
| | Claims <u>NONE</u> | NO |
| Inventive Step (IS) | Claims <u>1-7 and 10-21</u> | YES |
| | Claims <u>NONE</u> | NO |
| Industrial Applicability (IA) | Claims <u>1-7 and 10-21</u> | YES |
| | Claims <u>NONE</u> | NO |

2. CITATIONS AND EXPLANATIONS (Rule 70.7)

Claims 1-7 and 10-21 meet the criteria set out in PCT Article 33(2)-(4), because the prior art does not teach or fairly suggest a transgenic nematode or fly that expresses an SREBP pathway protein and because said transgenic nematode or fly can be used for studying lipid metabolism.

----- NEW CITATIONS -----

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.

PCT/US00/15880

VIII. Certain observations on the international application

The following observations on the clarity of the claims, description, and drawings or on the questions whether the claims are fully supported by the description, are made:

The description is objected to under PCT Rule 66.2(a)(v) as lacking clarity under PCT Article 5 because it fails to contain an adequate written description of practicing the claimed invention. The description is inadequate because: the description does not provide sufficient guidance as to how an artisan would have made and used any and all flies or nematodes (except *C.elegans* and a *drosophila melanogaster*) that expressed or mis-expressed any and all SREBP pathway proteins. It is noted that the art of making transgenic animals (flies and nematodes) is highly unpredictable due to several reasons, such as the site of integration of the transgene, expression level and pattern of the transgene, functional of the promoter used etc.

Claims 17 and 10-21 are objected to as lacking clarity under PCT Rule 66.2(a)(v) because practice of the claimed invention is not enabled as required under PCT Rule 5.1(a) for the reasons set forth in the immediately preceding paragraph.

Claims 4, 5, and 17 are objected to under PCT Rule 66.2(a)(v) as lacking clarity under PCT Article 6 because claims 4 and 17 are indefinite for the following reason(s): Claim 17 is indefinite because it recites the trademark name BODIPY. The claims scope is uncertain since the trademark or trade name can not be used properly to identify any particular material or product and because a trademark is used to identify a source of goods, not the goods themselves. In the instant case, the trademark/trade name is used to identify/describe a fluorescently-labeled fatty acid conjugate and, accordingly, the identification/description is indefinite. Claim 4 is indefinite because the term "said promoter" does not have antecedent basis, since the base claim recites the term "a heterogeneous promoter."

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US00/15880

| A. CLASSIFICATION OF SUBJECT MATTER | | |
|---|---|--|
| IPC(7) : A01K 67/00, 33/00; G01N 33/00 US CL : 800/3, 8, 13 According to International Patent Classification (IPC) or to both national classification and IPC | | |
| B. FIELDS SEARCHED | | |
| Minimum documentation searched (classification system followed by classification symbols) U.S. : 800/3, 8, 13 | | |
| Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched | | |
| Electronic data base consulted during the international search (name of data base and, where practicable, search terms used) MEDLINE,CAPLUS,USPATFUL | | |
| C. DOCUMENTS CONSIDERED TO BE RELEVANT | | |
| Category* | Citation of document, with indication, where appropriate, of the relevant passages | Relevant to claim No. |
| Y | ROSENFELD, J.M. et al. HLH106, a Drosophila sterol regulatory element-binding protein in a natural cholesterol auxotroph. The Journal of Biological Chemistry. 26 June 1998, Vol. 273, pages 16112-16121, see the entire document. | 1-7 and 10-21 |
| Y | SHIMOMURA I. et al. Nuclear sterol regulatory element-binding protein activates genes responsible for the entire program of unsaturated fatty acid biosynthesis in transgenic mouse liver. The Journal of Biological Chemistry. 25 December 1998, Vol. 273, pages 35299-35306, see the entire document. | 1-7 and 10-21 |
| <input checked="" type="checkbox"/> Further documents are listed in the continuation of Box C. <input type="checkbox"/> See patent family annex. | | |
| * Special categories of cited documents: | *T* | later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention |
| *A* document defining the general state of the art which is not considered to be of particular relevance | *X* | document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone |
| *B* earlier document published on or after the international filing date | *Y* | document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art |
| *L* document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified) | *G* | document member of the same patent family |
| *O* document referring to an oral disclosure, use, exhibition or other means | | |
| *P* document published prior to the international filing date but later than the priority date claimed | | |
| Date of the actual completion of the international search 31 JULY 2000 | Date of mailing of the international search report 18 SEP 2000 | |
| Name and mailing address of the ISA/US Commissioner of Patents and Trademarks Box PCT Washington, D.C. 20231 Facsimile No. (703) 305-3230 | Authorized officer RAM R. SHUKLA Telephone No. (703) 305-1677 | |

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US00/15880

| C (Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT | | |
|---|--|-----------------------|
| Category* | Citation of document, with indication, where appropriate, of the relevant passages | Relevant to claim No. |
| Y | SHIMANO, H. et al. Elevated levels of SREBP-2 and cholesterol synthesis in livers of mice homozygous for a targeted disruption of the SREBP-1 gene. Journal of Clinical Investigation. 1997, Vol. 100, pages 2115-2124, see the entire document. | 1-7 and 10-21 |

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US00/15880**Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)**

This international report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:
2. ☒ Claims Nos.: 8-9 AND 22-31
because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:

These claims contain nucleic acid and protein sequence information, however, no nucleic acid and protein sequence information was available.
3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1. ☐ As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest.
☐ No protest accompanied the payment of additional search fees.